

CLAIMS

What is claimed is:

1. A method of selectively detecting COX-2 activity in a sample, comprising:
 - a. adding a COX-2 selective substrate to the sample; and
 - b. detecting a metabolite of the COX-2 selective substrate, thereby indicating the COX-2 activity.
2. A method of measuring COX-1 activity in a sample, comprising:
 - a. adding a nonselective COX substrate and a COX-2 selective substrate to the sample;
 - b. allowing a period of time to pass;
 - c. measuring a first amount of a metabolite of the COX-1 substrate in the sample and a second amount of a metabolite of the COX-2 selective substrate metabolite; and
 - d. comparing the first amount and the second amount.
3. A method of detecting an activity of a COX-2 enzyme in a sample, comprising: detecting a PGH₂-EA metabolite in the sample, wherein the presence of the PGH₂-EA metabolite in the sample indicates the activity of the COX-2 enzyme.
4. A method of measuring an activity of a COX-2 enzyme in a sample, comprising:
 - a. quantifying an amount of a PGH₂-EA metabolite in the sample; and
 - b. relating the amount of the PGH₂-EA metabolite to the activity of the COX-2 enzyme.
5. A method of distinguishing a COX-2 activity from a COX-1 activity in a subject, comprising:
 - a. administering a COX-1 substrate and COX-2 selective substrate to the subject;
 - b. allowing a period of time to pass;
 - c. obtaining a sample from the subject;

- d. determining a first amount of a metabolite of the COX-1 substrate and a second amount of a metabolite of the COX-2 selective substrate; and
- e. comparing the first amount to the second amount.
6. A method of detecting an activity of a COX-2 enzyme in a subject, comprising:
 - a. obtaining a sample of the subject; and
 - b. detecting a PGH₂-EA metabolite in the sample, wherein the presence of the PGH₂-EA metabolite in the sample indicates the activity of the COX-2 enzyme in the subject.
7. The method of Claim 6, wherein the PGH₂-EA metabolite is selected from the group consisting of PGB₂-EA, PGD₂-EA, PGE₂-EA, PGF₂α-EA, TxB₂-EA, 6-keto-PGF₁α-EA, 15-keto-PGE₂-EA, 13,14-dihydro-15-keto-PGE₂-EA, PGG₂-EA, PGH₂-EA, PGA₂-EA, PGJ₂-EA, PGJ₂-EA derivatives, bicyclo-PGE₂-EA, 6-keto-PGF₁α-EA, TxA₂-EA and PGI₂-EA.
8. The method of Claim 6, wherein the subject is a mammal.
9. The method of Claim 6, wherein the sample is urine.
10. The method of Claim 6, wherein the sample is selected from a group consisting of: blood, plasma, cerebrospinal fluid, saliva, sputum, bile, joint fluid, biopsy, and conditioned media from a cell culture.
11. The method of Claim 6, wherein the detecting step further comprises generating a mass chromatogram of the PGH₂-EA metabolites.
12. The method of Claim 6, wherein the detecting step includes an immunoassay step.
13. A method of measuring an activity of a COX-2 enzyme in a subject, comprising:
 - a. obtaining a sample of the subject;
 - b. measuring an amount of a PGH₂-EA metabolite in the sample; and
 - c. relating the amount measured to the activity of the COX-2 enzyme.

14. The method of Claim 13, wherein the relating step further comprises comparing the amount measured to a standard value.
15. The method of Claim 13, wherein the relating step further comprises generating a standard curve.
- 5 16. The method of Claim 13, wherein the PGH₂-EA metabolite is selected from the group consisting of PGB₂-EA, PGD₂-EA, PGE₂-EA, PGF₂α-EA, TxB₂-EA, 6-keto-PGF₁α-EA, 15-keto-PGE₂-EA, 13,14-dihydro-15-keto-PGE₂-EA, PGG₂-EA, PGH₂-EA, PGA₂-EA, PGJ₂-EA, PGJ₂-EA derivatives, bicyclo-PGE₂-EA, 6-keto-PGF₁α-EA, TxA₂-EA and PGI₂-EA.
17. The method of claim 13, wherein the subject is a mammal.
18. The method of claim 13, wherein the sample is urine.
19. The method of claim 13, wherein the sample is selected from a group consisting of: blood, plasma, cerebrospinal fluid, saliva, sputum, bile, joint fluid, biopsy, and conditioned media from a cell culture.
20. The method of Claim 13, wherein the detecting step further comprises generating a mass chromatogram of the PGH₂-EA metabolites.
21. The method of Claim 13, wherein the detecting step includes an immunoassay step.
22. A method of screening for a tumor in a subject in need thereof, comprising:
- 20 a. obtaining a sample of the subject; and
- b. detecting a PGH₂-EA metabolite in the sample; wherein the presence of the PGH₂-EA metabolite is indicative of the tumor in the subject.
23. A method of screening for a tumor in a subject in need thereof, comprising:
- a. obtaining a sample of the subject;
- 25 b. measuring an amount of a PGH₂-EA metabolite in the sample; and
- c. relating the amount measured to an existence of the tumor.
24. A method of monitoring an anticancer treatment, comprising:

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- a. obtaining a first sample of a patient;
 - b. measuring a first amount of PGH₂-EA metabolite in the first sample;
 - c. obtaining a second sample from the patient after the patient undergoes anticancer therapy;
 - d. measuring a second amount of the PGH₂-EA metabolite in the second sample; and
 - e. determining a change in the second amount relative to the first amount, wherein the change determined is indicative of the effectiveness of the anticancer treatment.
- 10 25. A method of detecting an inflammation in a subject in need thereof, comprising:
- a. obtaining a sample of the subject; and
 - b. detecting an amount of a PGH₂-EA metabolite in the sample, wherein an inflammation is indicated when the amount detected equals or exceeds a threshold value.
- 15 26. A method of measuring an inflammation in a subject in need thereof, comprising:
- a. obtaining a sample of the subject; and
 - b. detecting an amount of a PGH₂-EA metabolite in the sample, wherein an inflammation is indicated when the amount measured equals or exceeds a threshold value.
- 20 27. A method of monitoring an anti-inflammation therapy in a subject in need thereof, comprising:
- a. obtaining a first sample from the subject;
 - b. measuring a first amount of a PGH₂-EA metabolite in the first sample;
 - c. obtaining a second sample from the patient after the anti-inflammation therapy;
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- d. measuring a second amount of the COX-2 specific metabolite in the second sample; and
- e. determining a change in the second amount relative to the first amount, wherein the change determined is indicative of the effectiveness of the anti-inflammation therapy.

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28. A composition comprising: a label for detecting a PGH_2 -EA metabolite.
29. The composition of Claim 28, further comprising an isolated PGH_2 -EA metabolite including an isotopic label.
30. The method of Claim 28, wherein the PGH_2 -EA metabolite is selected from the group consisting of PGB_2 -EA, PGD_2 -EA, PGE_2 -EA, $\text{PGF}_{2\alpha}$ -EA, TxB_2 -EA, 6-keto- $\text{PGF}_{1\alpha}$ -EA, 15-keto- PGE_2 -EA, 13,14-dihydro-15-keto- PGE_2 -EA, PGG_2 -EA, PGH_2 -EA, PGA_2 -EA, PGJ_2 -EA, PGJ_2 -EA derivatives, bicyclo- PGE_2 -EA, 6-keto- $\text{PGF}_{1\alpha}$ -EA, TxA_2 -EA and PGI_2 -EA.
31. The composition of Claim 28, further comprising an isolated PGH_2 -EA metabolite including a non-positron emitting isotopic label.
32. The composition of Claim 28, further comprising an isolated PGH_2 -EA metabolite including an isotopic label selected from the group consisting of ^2H , ^3H , ^{13}C , and ^{14}C .
33. The composition of Claim 28, further comprising an PGH_2 -EA metabolite including a fluorescent label.
34. A process for making an isolated PGH_2 -EA metabolite including a label comprising: reacting a COX-2 metabolite with a labeled ethanolamide.
35. The process of Claim 34, wherein the label is isotopic.
36. The process of Claim 34, wherein the label is nonpositron emitting.
37. The process of Claim 34, wherein the label is selected from the group consisting of ^2H , ^3H , ^{13}C , and ^{14}C .
38. The process of Claim 34, wherein the label is fluorescent.

39. A process for making an isolated PGH₂-EA metabolite including a label comprising: reacting a labeled COX-2 metabolite with ethanolamide.
40. The process of Claim 39, wherein the label is isotopic.
41. The process of Claim 39, wherein the label is nonpositron emitting.
- 5 42. The process of Claim 39, wherein the label is selected from the group consisting of ²H, ³H, ¹³C, and ¹⁴C.
43. The process of Claim 39, wherein the label is fluorescent.
44. An article of manufacture comprising, packaged together:
- a. a vessel containing an isolated antibody against a PGH₂-EA metabolite; and
 - b. a set of instructions delineating a process of measuring a COX-2 specific activity.
45. An article of manufacture comprising, packaged together:
- a. a vessel containing at least one labeled PGH₂-EA metabolite; and
 - b. a set of instructions delineating a process of measuring a COX-2 specific activity.
46. An antibody that binds specifically to a COX-2 metabolite ethanolamide.
47. An antibody that binds specifically to a PGH₂-EA metabolite.
48. An antibody that binds specifically to a PGE₂ ethanolamide.
- 20 49. A process of making an antibody that binds specifically to PGH₂-EA metabolites from a prostaglandin with substituted cyclopentyl and amide moieties, comprising:
- a. protecting the cyclopentyl substituents and ethanolamide moiety of the prostaglandin to produce a protected PG-EA;
 - 25 b. chemically modifying the protected PG-EA with an appropriate conjugate to produce a protected, conjugated PG-EA;
 - c. deprotecting the conjugated PG-EA to generate an immunogen; and

d. purifying the immunogen.

50. A method of measuring an activity of a COX-2 enzyme in a subject, comprising:

a. administering an amount of a AEA to the subject;

b. obtaining a sample of the subject;

5 c. measuring an amount of a PGH₂-EA metabolites in the sample; and

d. relating the amount of the PGH₂-EA metabolites to the activity of the COX-2 enzyme.

51. The method of Claim 50, wherein the AEA includes a label.

52. The method of Claim 50, further comprising the step of comparing the amount measured to a standard.

53. A composition comprising: a prostaglandin D₂-ethanolamide and pharmaceutically acceptable salts thereof.

54. A composition comprising: a 6-keto-prostaglandin F_{1α}-ethanolamide and pharmaceutically acceptable salts thereof.